



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

MU

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/705,432

11/10/2003

Wojtek Auerbach

REG 784

4884

26693

7590

05/24/2006

REGENERON PHARMACEUTICALS, INC  
777 OLD SAW MILL RIVER ROAD  
TARRYTOWN, NY 10591

EXAMINER

MONTANARI, DAVID A

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 05/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

10/705,432

Applicant(s)

AUERBACH ET AL.

Examiner

David Montanari

Art Unit

1632

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 5 May 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: NONE.  
Claim(s) objected to: NONE.  
Claim(s) rejected: 9 and 15-24.  
Claim(s) withdrawn from consideration: NONE.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: \_\_\_\_\_.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_.  
13. ☒ Other: See Continuation Sheet.

Continuation of 13. Other: Applicants arguments and amendments filed 5/5/2006 have been entered. The rejection of claims 17-20 under 35 USC 112, first paragraph is withdrawn. Applicants argue in amendment that 103(a) rejection of claims 9 and 15-24 lacks the requisite teachings and motivations by the art of record to make and use the claimed invention. Applicants argue that nothing in the art of record suggests the combination of a targeting vector and a ubiquitin promoter, and specifically nothing in the art of record suggests a method of improving targeting efficiency. These arguments are not persuasive. The issue of improving targeting efficiency is a moot point since there is no recitation in the claims of an "improved method". Art is used to reject the claims, the "improved method" is taught in the specification, and is not the issue in the instant 103(a) rejection. Next, the combination of Rohozinski and Tsirigotis provide ample motivation to the ordinary artisan. Rohozinski goes into detail about targeting specific chromosomal locations in mouse ES cells via homologous recombination. Tsirigotis, particularly details the beneficial effects of using the ubiquitin promoter to drive gene expression. The ubiquitin promoter, is "ubiquitis", meaning it is expressed in all cells and tissues, and thus an exemplary promoter for gene targeting. A thorough reading of Tsirigotis would provide ample motivation to the ordinary artisan to use the ubiquitin promoter in many gene targeting experiments, including gene targeting via homologous recombination. The addition of Ghazizadeh further teaches and motivates the ordinary artisan to use drug resistance genes to select transformed cells that are expressing a transgene of interest. A combination of these three references provides all of the necessary requisites to the ordinary artisan to make and use the claimed invention. Thus for reasons of record in the office action mailed 3/2/2005 and above the rejection is maintained .



**DAVE TRONG NGUYEN**  
**SUPERVISORY PATENT EXAMINER**